AR201-13590A

HIGH PRODUCTION VOLUME (HPV)

CHEMICAL CHALLENGE PROGRAM

TEST PLAN

For The

ALKYL ALCOHOLS C6 - C13 CATEGORY

CAS# 68526-79-4: Hexanol, branched and linear
CAS# 70914-20-4: Alcohols C6-8, branched
CAS# 68526-83-0: Alcohols C7-9 iso, C8 rich
CAS# 68526-84-1: Alcohols C8-10 iso, C9 rich
CAS# 68526-85-2: Alcohols C9-11 iso, C10 rich
CAS# 68526-86-3: Alcohols C11-14 iso, C13 rich

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EXECUTIVE SUMMARY

Under EPA's High Production Volume (HPV) Chemical Challenge Program, ExxonMobil Chemical Company has committed to voluntarily compile a Screening Information Data Set (SIDS) on a category of chemicals defined as Alkyl Alcohols C6 - C13. This category is supported by the basic screening data needed for an initial assessment of the physicochemical properties, environmental fate, and human and environmental effects of chemicals as defined by the Organization for Economic Cooperation and Development (OECD). The information used to complete the HPV SIDS endpoints comes from existing data.

ExxonMobil Chemical Company believes a category of Alkyl Alcohols C6 - C13 is scientifically justifiable because their physicochemical and toxicological properties are very similar and follow a regular pattern as a result of the synthesis process. The structural similarity of the component chemicals from these products creates a predictable pattern in the following parameters: physicochemical properties, environmental fate and environmental effects, and human health effects. The similarities are based on the following:

- A common structure represented by RCOH,
- An incremental and constant change across the category where R is a branched alkyl group having carbon numbers C5, C6, C7, C8, C9, C11, or C12 as the main constituent, and
- A likelihood of common precursors and breakdown products that can result in structurally similar metabolites (e.g. carboxylic acid).

This test plan is based on the observation that the toxicological properties are similar or vary in an incremental and predictable fashion within the category.

The test data compiled for the category anchor studies proves adequate to support a screening-level hazard assessment for the category and its members (CAS numbers, 68526-79-4, 70914-20-4, 68526-83-0, 68526-84-1, 68526-85-2, and 68526-86-3). The untested endpoints can be assessed by interpolation between data from the category anchor studies.

Substantial amounts of data exist to evaluate selected potential hazards of Alkyl Alcohols C6-C13. To complete the health hazard assessment of the category, a mouse micronucleus assay will be conducted on Alkyl Alcohol C6 and compared to clastogenicity data on other category members. The ecological hazard assessment will be completed by conducting an acute algal toxicity study on the C6 (68526-79-4) and C13 (68526-86-3) alkyl alcohols.

Evaluation of the Alkyl Alcohols C6 - C13 as a category has several advantages. All products in this category can be adequately characterized for the HPV endpoints by using a matrix of completed studies for members in the category. By using this approach, the safety of the category can be determined without having to conduct tests for every endpoint with every chemical. Not only will this inform the public about the potential hazards of Alkyl Alcohols C6 - C13, but it will also reduce the number of animals that would be required to evaluate the toxicity of individual members of the Alkyl Alcohols C6 - C13 Category.

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TEST PLAN FOR ALKYL ALCOHOLS C6 - C13

I. INTRODUCTION

Under EPA's High Production Volume (HPV) Chemical Challenge Program, ExxonMobil Chemical Company has committed to voluntarily compile a Screening Information Data Set (SIDS) on a category of chemicals defined as Alkyl Alcohols C6 - C13. This category is supported by the basic screening data needed for an initial assessment of the physicochemical properties, environmental fate, and human and environmental effects of chemicals as defined by the Organization for Economic Cooperation and Development (OECD). The information used to complete the SIDS endpoints comes from existing data and fulfills an ExxonMobil obligation to the HPV Challenge Program.

ExxonMobil Chemical Company believes a category of Alkyl Alcohols C6 - C13 is scientifically justifiable because their physicochemical and toxicological properties are very similar and follow a regular pattern as a result of the synthesis process. The structural similarity of the component chemicals from these products creates a predictable pattern in the following parameters: physicochemical properties, environmental fate and effects, and human health effects. The similarities are based on the following:

- A common structure represented by RCOH,
- An incremental and constant change across the category where R is a branched alkyl group having carbon numbers C5, C6, C7, C8, C9, C11, or C12 as the main constituent, and
- A likelihood of common precursors and breakdown products that can result in structurally similar metabolites (e.g. carboxylic acid).

This test plan is based on the observation that the toxicological properties are similar or vary in an incremental and predictable fashion within the category.

The test data compiled for the category proves adequate to support a screening-level hazard assessment for the category and its members (CAS numbers, 68526-79-4, 70914-20-4, 68526-83-0, 68526-84-1, 68526-85-2, and 68526-86-3). The untested endpoints can be assessed by interpolation between data from the category anchor studies. The existing data suggest that products in the Alkyl Alcohols C6 - C13 Category exhibit relatively low toxicity for human health endpoints and moderate to high toxicity for the environmental health endpoints.

A substantial amount of data exists to evaluate the potential hazards of Alkyl Alcohols C6-C13. To complete the health hazard assessment of the category, a mouse micronucleus assay will be conducted on Alkyl Alcohol C6 and compared to clastogenicity data on other category members. The ecological hazard assessment will be completed by conducting an acute algal toxicity study on the C6 (68526-79-4) and C13 (68526-86-3) alkyl alcohols.

The data from this category will be used to inform the public about the potential hazards of the Alkyl Alcohols C6 - C13. Developing a data matrix of anchor studies and applying justifiable read across practices will provide a sufficiently robust data set to

characterize each endpoint in the HPV Chemical Challenge Program without having to conduct a test for each endpoint and product. This resourceful use of existing data will result in fewer animals needed for testing purposes while adequately assessing the potential hazards of products in the Alkyl Alcohol C6 - C13 Category.

II. CHEMICAL PROCESS AND DESCRIPTION

The Alkyl Alcohols C6 - C13 Category contains a group of alkyl alcohol products whose physicochemical and toxicological properties are very similar and follow a regular pattern as a result of synthesis and structural similarity (Table 1). The production of alkyl alcohol products involves the reaction between a branched olefin and a mixture of carbon monoxide and hydrogen to produce an aldehyde, which is then hydrogenated to yield the alcohol.

The structural similarity of chemcials in the products of this category creates a predictable pattern in the following parameters: physicochemical properties, environmental fate and effects, and human health effects. The structural features of members of the category are as follows:

- A common structure - ROH,
- An incremental and constant change across the category where R is a branched alkyl group having carbon numbers of C6, C7, C8, C9, C10, C12, or C13 as the main constituent,
- A common functional hydroxyl group, and
- A likelihood of common precursors and breakdown products which result in structurally similar chemicals (e.g., carboxylic acid).

Table 1. CAS Numbers and Descriptions

CAS Number	Chemical Name	Generic Name
68526-79-4	Hexanol, branched and linear	Hexyl alcohol
70914-20-4	Alcohols C6-8, branched	Isoheptyl alcohol
68526-83-0	Alcohols C7-9, branched*	Isooctyl alcohol
68526-84-1	Alcohols C8-10 iso, C9 rich	Isononyl alcohol
68526-85-2	Alcohols C9-11 iso, C10 rich	Isodecyl alcohol
68526-86-3	Alcohols C11-14 iso, C13 rich	Tridecyl alcohol

* = Not currently HPV but included to facilitate category evaluation

Evaluation of the Alkyl Alcohols C6 - C13 as a category accomplishes the goal of the HPV Program - to obtain screening level hazard information - through the strategic selection of products within this category. The testing strategy is based on the principle that:

- These products behave in a similar and/or predictable manner, and
- Interpolation of data can be used to assess the alkyl alcohol products for which data are not available.

Procedures to assess the reliability of selected studies described in this test plan are based on the guidelines described by Klimisch *et al.*, 1997.

III. TEST PLAN RATIONALE

A. Physicochemical Data

Physicochemical data (i.e., melting point, boiling point, vapor pressure, water solubility, and Kow) for selected chemical components in the Alkyl Alcohol C6 - C13 category will be calculated using the EPIWIN© model (EPIWIN, 1999), as discussed in the EPA document titled "The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program." These data will be presented as ranges, based on the chemical components selected to represent each alkyl alcohol product. In addition, measured data for some of these endpoints will also be provided for selected alkyl alcohol products where readily available. Where possible, the measured and calculated data will be presented together for comparative purposes.

Table 2 lists selected measured physicochemical data (boiling range, vapor pressure, and specific gravity) as they appear on the material safety data sheets for products in this category. These data are provided with this test plan to further justify these products as a distinct category under the HPV Program. Also included are calculated and measured values for water solubility and K_{ow}. As shown by the data in Table 2, the structural similarity of the alkyl alcohol products results in a predictable and incrementally increasing pattern of physiochemical properties from the C6 to C13 rich products.

Table 2. Selected Physical Properties of Alkyl Alcohols C6 - C13

CAS NUMBER	CHEMICAL NAME	BOILING RANGE (° C)	VAPOR PRESSURE (mm Hg @ 100° C)	SPECIFIC GRAVITY	WATER SOLUBILITY (Mg/L)	LOG K_{ow}
68526-79-4	Hexanol, branched and linear	152 - 163	124	0.82	10,340 - 11,950[a]	1.8 - 2.0[a]
70914-20-4	Alcohols C6-8, branched	167 - 176	78	0.83	3,539 - 11,950[a]	1.8 - 2.6[a]
68526-83-0	Alcohols C7-9, branched*	185 - 193	27	0.83	1,379 - 1,485[a]	2.9 - 3.4[b]
68526-84-1	Alcohols C8-10 iso, C9 rich	203 - 215	16	0.84	164 - 614[a]	3.4 - 3.9[b]
68526-85-2	Alcohols C9-11 iso, C10 rich	217 - 224	8.2	0.84	75.0[b]	3.8[b]
68526-86-3	Alcohols C11-14 iso, C13 rich	256 - 266	2.7	0.84	5.8[b]	4.2 - 5.0[b]

* = Not currently HPV but included to facilitate category evaluation
[a] Calculated using EPIWIN
[b] Measured values (Robust summaries are attached)

B. Human Health Effects

ExxonMobil Chemical Company believes the category of Alkyl Alcohols C6 - C13 is scientifically justifiable. Furthermore, we believe that the test data compiled for the category proves adequate to support a screening-level hazard assessment of potential health hazards for the category and its members (CAS numbers, 68526-79-4, 70914-20-4, 68526-83-0, 68526-84-1, 68526-85-2, and 68526-86-3). Table 3 summarizes the proposed test plan for the category. Because of the common structure and predictable toxicity of members of the category, one can assess the untested endpoints by extrapolation between and among the category members.

Metabolism

Alkyl Alcohols would likely be broken down by mitochondrial beta-oxidation or by cytochrome P450 mediated omega and omega-minus-one oxidation (may be followed by beta-oxidation). The alcohol undergoes various oxidative steps to yield other alcohols, ketones, aldehydes, carboxylic acids and carbon dioxide (Mann, 1987). Data for monohydric, aliphatic alcohols show a systematic variation according to molecular weight in a manner similar to many other homologous series (Monick, 1968). The body handles aliphatic hydrocarbons in a similar manner via oxidative conversion to alcohols, ketones, and eventual elimination as carbon dioxide and carboxylic acids (Wislocki et al, 1980). The undegraded alcohols can be conjugated either directly or as a metabolite with glucuronic acid, sulfuric acid, or glycine and are rapidly excreted (Lington and Bevan, 1994). Intermediate aldehydes could be reactive and bind with DNA and/or proteins. Glucuronidation and glutathione conjugation are possible means of rapid elimination (Mann, 1987).

C. Presentation of Alkyl Alcohols C6 - C13 Category Health Effects Data Associated with the Anchor Studies under the HPV Challenge Program

Acute Oral Toxicity

TEST	Hexanol, branched and linear	Alkyl alcohol C6-8, branched	Alkyl alcohol C7-9, branched	Alkyl alcohol C8-10, branched	Alkyl alcohol C9-11, branched	Alkyl alcohol C11-14, branched
ACUTE ORAL - RAT	=3.7 g/kg (Hazleton, 1960)	>3.9 g/kg (Esso, 1979a)	>2 g/kg (RCC, 1988a)	=3.0 g/kg (Esso, 1968b)	=4.6 g/kg (Esso, 1960a)	>2 g/kg (RCC b,c)

All of the Alkyl Alcohols C6 - C13 have a low order of toxicity to rats via the oral route of exposure. The LD_{50} for the C6 branched and linear alkyl alcohol anchor study was >3.7 g/kg. The LD_{50}'s for the C6-C8, C7-C9, C8-C10, C9-C11, and C11-C14 branched alkyl alcohols were all > 2 g/kg. For all members of the category, acute oral exposure induced signs of systemic toxicity that were characterized by depression, sedation, and ataxia. These results demonstrate that members of the alkyl alcohol category have a consistent, low order of acute oral toxicity.

Acute Dermal Toxicity

TEST	Hexanol, branched and linear	Alkyl alcohol C6-8, branched	Alkyl alcohol C7-9, branched	Alkyl alcohol C8-10, branched	Alkyl alcohol C9-11, branched	Alkyl alcohol C11-14, branched
ACUTE DERMAL - RABBIT	>2.6 g/kg (Hazleton, 1960)	>3.16 g/kg (Esso, 1979b)	>2.6 g/kg (Hazleton, 1960)	>3.16 g/kg (Esso, 1968c)	>2.6 g/kg (Esso, 1960b)	RA

The Alkyl Alcohols C6 - C13 have a low order of toxicity via the dermal route of exposure. The rabbit dermal LD_{50} for all members of the category was greater than 2.6 g/kg. This indicates that the members of this category have a consistent pattern of acute toxicity via the dermal route of exposure.

Genotoxicity

TEST	Hexanol, branched and linear	Alkyl alcohol C6-8, branched	Alkyl alcohol C7-9, branched	Alkyl alcohol C8-10, branched	Alkyl alcohol C9-11, branched	Alkyl alcohol C11-14, branched
AMES - S. typhimurium; TA98, 100, 1535, 1537, 1538 ± Activation	NEGATIVE (1-hexanol) (ECB, 2000a)	RA	NEGATIVE (2-ethyl-1-hexanol) (Shimizu, 1985, ECB, 2000b)	RA	RA	NEGATIVE (1-dodecanol) (ECB, 2000c)
Chromosomal Aberration - In Vitro or In Vivo	ND	ND	NEGATIVE (2-ethyl-1-hexanol) (ECB, 2000b)	ND	ND	NEGATIVE (1-dodecanol) (ECB, 2000c)

RA Read Across
ND No Data

In Vitro

An evaluation of the genotoxic potential of Alkyl Alcohols C6 - C13 is based on the existing data for structural isomers as well as on data from metabolic precursors. The weight of evidence from this existing data supports the conclusion that these materials are not genotoxic and obviates the need for further testing.

Existing data on 1-hexanol, which is an isomer of Alkyl Alcohol C6, indicates that this material is not genotoxic. In addition, 2-ethyl-1-hexanol and 1-dodecanol were evaluated in Ames Assays in the presence and absence of metabolic activation. The 2-ethyl-1-hexanol is an isomer of Alkyl Alcohol C7-C9, and the 1-dodecanol is an isomer of Alkyl Alcohol C11-C14. Both materials were not mutagenic in Ames assays using five strains of *Salmonella typhimurium*. IUCLID files for 1-hexanol, 2-ethyl-1-hexanol, and 1-dodecanol are publicly available in the European Chemicals Bureau (ECB) IUCLID database and are included with this submission (ECB, 2000).

Further data to support the hazard assessment for the category comes from a series of Alkyl Acetates C6-C13. These materials have also been shown to be non-genotoxic in the Ames assay (EBSI, 1995a; 1994b,c). Alkyl Acetates are manufactured from the Alkyl Alcohols and undergo metabolism by esterases to produce acetic acid and the corresponding Alkyl Alcohol. As indicated in a previous test plan submitted for the Alkyl Acetates, there is no evidence for genotoxicity with these compounds in a variety of strains of *S. typhimurium* in the presence or absence of metabolic activation. The C6, C6-C8, C7-C9, and C11-C14 Alkyl Acetates, all of which are metabolized to the corresponding Alkyl Alcohol, produced negative results in the Ames test. These data, in conjunction with the negative data on structural isomers of these materials provide strong evidence that Alkyl Alcohols are not genotoxic.

In Vivo

Based on existing data for structurally similar materials, members of the Alkyl Alcohols C6 -C13 category are not expected to be clastogenic. However, while sufficient evidence exists for the higher molecular weight members of the Alkyl Alcohols C6 -C13 category, there is less evidence for the lack of clastogenic activity for the low molecular weight members (i.e. Alkyl Alcohol C6). Therefore, to complete the category evaluation, we will conduct a mouse micronucleus assay on Alkyl Alcohol C6 (68526-79-4). This result will be compared to the results to clastogenicity tests already conducted on structural isomers and similar materials.

In a mouse micronucleus assay, 1-dodecanol produced negative results. Furthermore, 2-ethyl-1-hexanol produced negative results in both a mouse micronucleus assay and a mouse lymphoma assay. In addition, 1-hexanol and 2-ethyl-1-hexanol were not oncogenic in chronic studies. IUCLID files for 1-hexanol, 2-ethyl-1-hexanol, and 1-dodecanol are publicly available in the European Chemicals Bureau (ECB) IUCLID database and are included with this submission (ECB, 2000).

As described before, the Alkyl acetates can be used to predict the clastogenic potential of the Alkyl Alcohols. These materials are metabolized to the corresponding alcohol. An Alkyl Acetate ester (C6) was not clastogenic in an *in vitro* chromosome aberration assay

in CHO cells (EBSI, 1995b). In addition, both a C7-C9 and C11-C14 Alkyl Acetate produced negative results in a mouse micronucleus assay (EBSI, 1994 d,e). Although there was evidence of cytotoxicity at extremely high doses, no clastogenic activity was observed. These results demonstrate that the Alkyl Acetates are not clastogenic and that they display a consistent pattern of toxicity when clastogenicity is evaluated as an endpoint.

Given the consistent pattern of toxicity displayed by members of the Alkyl Alcohol family, we feel that it is not necessary to systematically evaluate the clastogenicity of all members of the Alkyl Alcohol category. Therefore, we feel it will be sufficient to conduct a mouse micronucleus test on Alkyl Alcohol C6 and compare the results of that test to the results of tests on other Alkyl Alcohol isomers and with the Alkyl Acetates. This strategy also addresses concerns of animal welfare by reducing the number of animals required to evaluate the category.

Subchronic Toxicity

TEST	Hexanol, branched and linear	Alkyl alcohol C6-8, branched	Alkyl alcohol C7-9, branched	Alkyl alcohol C8-10, branched	Alkyl alcohol C9-11, branched	Alkyl alcohol C11-14, branched
ORAL - Rat	NOAEL (rat, dog) ≥ 0.5% in diet (ECB, 2000a) Repeat Dermal Application* NOAEL = 2.0 g/kg/day (Esso, 1961a)	RA	Subacute gavage* NOAEL = 130 mg/kg/day; (Rhodes, 1984) Subchronic gavage NOEL = 125 mg/kg/day; LOEL = 250 mg/kg/day (ECB, 2000b) Repeat Dermal Application* NOAEL = 2.0 g/kg/day (Esso, 1961b)	Subacute gavage* NOAEL = 144 mg/kg/day (Rhodes, 1984)	RA	Subchronic Feed NOEL = 100 mg/kg/day (1-dodecanol, ECB 2000c)

* Referenced Supportive Internal Study Document (Reliable with restrictions)

An evaluation of the publicly available repeated dose studies indicates that Alkyl Alcohols C6 - C13 have a low order of subchronic toxicity. Subchronic toxicity data on 1-hexanol, an isomer of Alkyl Alcohol C6, indicates that this material has a low order of subchronic toxicity. Thirteen-week dietary feeding studies in both the rat and dog produced a NOAEL greater than or equal to 0.5% in the diet. Furthermore, a number of studies have evaluated the toxicity of repeated exposure to 2-ethylhexanol, an isomer of Alkyl Alcohol C7-9. In a 3-month study in rats, 2-ethylhexanol was administered by oral gavage at doses of 25, 125, 250, and 500 mg/kg/day. At the highest doses (250 and 500 mg/kd/day), changes in body and organ weights were observed. The NOEL for the study was 125 mg/kg/day and the LOEL for the study was 250 mg/kg/day based on body weight changes. Finally, an OECD 422 oral feed study on 1-dodecanol at doses of 100, 500, and 2000 mg/kg/day produced a NOEL of 100 mg/kg/day based on a

reduction in mean white blood cell count. However, no other effects were observed in gross or histological examinations. Summaries of the subchronic studies on 1-hexanol, 2-ethylhexanol, and 1-dodecanol are publicly available from the European Chemicals Bureau (ECB) IUCLID database and are included with this submission (ECB, 2000).

A 14-day oral study was conducted in Wistar rats with iso-octanol and isononanol at doses of 130 mg/kg/day and 144 mg/kg/day, respectively. Plasma cholesterol and triglycerides were analyzed, the testes and liver were weighed, and the liver was analyzed for both histopathological lesions and the activity of peroxisomal enzymes. No treatment-related effects were observed during the study. Neither iso-octanol nor isononanol induced any significant changes in testes or liver weight, vacuolation, or activity of the peroxisome-associated enzymes. The NOAEL for iso-octanol was the limit dose of 130 mg/kg/day and the NOAEL for isononanol was the limit dose of 144 mg/kg/day.

Dermal exposure of rats to 0.4 and 2.0 g/kg/day hexyl alcohol or Alkyl alcohol C7 - 9, branched for 10 days resulted in no clinical signs of toxicity at any time during the study. All animals survived to study termination and there were no treatment-related clinical, in-life, gross postmortem or microscopic findings. The no observable adverse effect level (NOAEL) for repeat dermal exposure was 2.0 g/kg/day.

Taken together, the results of these studies demonstrate that Alkyl Alcohols C11-C14 have a low order or toxicity under conditions of repeat exposure by both the oral and dermal routes. In addition, they demonstrate that the members of the category display a consistent degree of subchronic toxicity by either the oral or dermal routes of exposure. Therefore, Alkyl Alcohols C6-C13 do not require further testing to assess subchronic toxicity.

Developmental Toxicity

TEST	Hexanol, branched and linear	Alkyl alcohol C6-8, branched	Alkyl alcohol C7-9, branched	Alkyl alcohol C8-10, branched	Alkyl alcohol C9-11, branched	Alkyl alcohol C11-14, branched
ORAL - Rat	(Inhalation) NOAEL = 3500 mg/m^3 (Nelson, 1989)	RA	DEV-TOX MATERNAL NOAEL = 500 mg/kg; FETAL NOAEL = 1000 mg/kg; (EBSI, 1994a) DEV-TOX (Inhalation) NOAEL = 400 mg/m^3 (Nelson, 1990)	DEV-TOX MATERNAL/ FETAL NOAEL = 144 mg/kg; (USEPA, 1989) DEV-TOX (Inhalation) NOAEL = 150 mg/m^3 (Nelson, 1990)	DEV-TOX MATERNAL NOAEL = 158 mg/kg; FETAL NOAEL = 790 mg/kg (USEPA, 1989b) DEV-TOX MATERNAL/ FETAL NOAEL = 1,440 mg/kg (USEPA, 1989b) DEV-TOX (Inhalation) NOAEL = 100 mg/m^3 (Nelson, 1990)	RA

*Referenced Supportive Internal Study Document (Reliable with restrictions)

Oral Exposure

Studies on the developmental toxicity of Alkyl Alcohols C6-C13 indicate that these materials have a lower order of toxicity and are not considered selective developmental toxicants by either the oral or inhalation routes of exposure. Alkyl alcohol C7-9, branched was orally administered at 100, 500, and 1000 mg/kg on gestation days 6-15 in a developmental toxicity study in rats. Maternal toxicity was seen in the high dose group as indicated by emaciation, rales, and hypoactivity. However, no adverse maternal effects were observed in the low or mid-dose groups. In addition, there were no significant signs of fetal toxicity in any of the dose groups. A maternal NOAEL of 500 mg/kg and a fetal NOAEL of 1000 mg/kg were observed.

In another study, the developmental toxicity of isononylalcohol 1 and isononylalcohol 2 were evaluated in Wistar rats. Isononyl 1 consists of isomers with a moderate degree of branching (dimethyl heptanols) and contains approximately 16% isodecanol. Isononyl 2 consists of isomers with a low degree of branching (dimethyl heptanols and methyl octanols). Each test substance was administered by oral gavage at 144, 720, or 1440 mg/kg/day during days 6-15 of gestation. At the middle and high dose levels of isononylalcohol 1, signs of maternal and fetal toxicity, including decreased body weight, were observed. At the lowest dose of isononylalcohol 1, no maternal toxicity was observed. There were an increased number of fetuses with hydroureter. However, the significance of this endpoint as an indicator of marginal developmental toxicity is questionable. Therefore, isononylalcohol 1 was considered to induce developmental toxicity only at doses that induce overt maternal toxicity. Isononylalcohol 2 also

produced maternal and fetal effects at both the middle and high doses. At the lowest dose however, no maternal or fetal toxicity was observed. Therefore, isononylalcohol 2 induced fetal toxicity at doses that also induce overt maternal toxicity. The maternal NOAEL for isononylalcohol 1 and isononylalcohol 2 is 144 mg/kg. The fetal NOAEL for isononylalcohol 1 is less than 144 mg/kg, whereas the fetal NOAEL for isononylalcohol 2 is 144 mg/kg.

In a similar study, the developmental toxicity of isodecanol (isomers of trimethyl heptanols and dimethyl octanols) was evaluated in Wistar rats by oral gavage at doses of 158, 790, and 1580 mg/kg during days 6-15 of gestation. Signs of compound-induced toxicity including reduced body weight were observed in dams of the middle and high dose groups. No maternal signs of toxicity were observed in the low dose group. Fetotoxic effects including reduced mean fetal body weight and skeletal retardations were observed only in the highest dose group. The maternal NOAEL for this study was 158 mg/kg and the fetal NOAEL was 790 mg/kg. Thus, isodecanol is fetotoxic only at doses that produce overt maternal toxicity.

An identical study conducted concurrently on C-7-9-11 alcohol (consists of isomers of heptanol, nonanol, and undecanol) produced negative results at all three dose levels tested: 144, 720, and 1440 mg/kg/day. No adverse effects were observed in dams or in the fetuses at any of these doses. The NOAEL for this study was therefore 1440 mg/kg/day.

Inhalation Exposure

The developmental toxicity resulting from inhalation of saturated vapors has also been evaluated for several members of the Alkyl Alcohols C6 - C13 category. Inhalation of Alkyl Alcohols C6-C13 is the primary concern during industrial use, particularly for the lower molecular weight members of the category. Therefore, an evaluation of inhalation studies is useful for evaluating the developmental toxicity of the category.

The available developmental toxicity data for structural isomers of the Alkyl Alcohols indicate that these materials are not developmentally toxic via the inhalation route of exposure. Inhalation of saturated vapors of 1-hexanol (3500 mg/m^3, 7 hr/day, GD 1-19) resulted in no significant signs of maternal or fetal toxicity. The NOAEL for both maternal and fetal effects for this study was the limit dose of 3500 mg/m^3.

Another study evaluated the developmental toxicity of three structurally related alcohols, 1-octanol, 1-nonanol, and 1-decanol following inhalation. Sprague-Dawley rats were exposed to saturated vapors of 1-octanol (400 mg/m^3), 1-nonanol (150 mg/m^3), and 1-decanol (100 mg/m^3) for 7 hours per day during days 1-19 of gestation. No significant effects, including no changes in maternal weight gain, feed consumption, or water intake were observed between the control and any of the treated groups. In addition, no fetal toxicity was observed, as indicated by fetal body weight, sex ratio, and the number of resorptions. The NOAEL for both maternal and fetal effects for each test substance was the saturated vapor concentration: 1-octanol (400 mg/m^3), 1-nonanol (150 mg/m^3), and 1-decanol (100 mg/m^3).

Collectively, the weight of evidence demonstrates that Alkyl Alcohols C6-C13 have a low order or maternal toxicity and do not induce signs of developmental toxicity until maternal toxicity is observed. Hence, these materials are not selective developmental toxicants. In addition, the maternal and fetal NOAELs for oral exposure to different members of the category are consistent. Furthermore, the NOAELs for inhalation reflect the maximum achievable vapor concentration. Since these materials are not selective toxicants and display a consistent, low order of developmental toxicity they will not undergo further testing for developmental toxicity.

Reproductive Toxicity

The available reproductive toxicity studies and repeat-dose studies prove adequate to support a screening-level hazard assessment for the reproductive toxicity potential of Alkyl Alcohols C6 - C13. Developmental toxicity studies conducted by the oral route of exposure on Isooctyl alcohol, Isononyl alcohol, Isodecanol, and Undecyl alcohol, produced consistent results and demonstrated that these materials do not affect reproductive parameters. Although a slight increase in resporptions was observed in several studies, this only occurred in the highest dose group and in the presence of overt maternal toxicity. Furthermore, inhalation exposure to saturated vapors of 1-hexanol, 1-octanol, 1-nonanol, and 1-decanol did not induce any significant changes in reproductive parameters. In the subacute studies of isooctyl alcohol and isononyl alcohol, no changes in testicular weight were observed. These data support the conclusion that the Alkyl Alcohols C6-C13 are not selective reproductive toxicants. According to the OECD SIDS Guidelines, adequate developmental toxicology data coupled with subchronic toxicity data that shows no effects on reproductive organs fulfills the requirement for an assessment of reproductive toxicity potential.

D. Aquatic Toxicity

The alkyl alcohol products ranging from hexanol, branched and linear, to C11-C14 iso, C13 rich, have been shown to produce an expected increasing level of acute toxicity to freshwater fish and invertebrates. This is based on data from the literature that are used to read across to selected alcohol products in this test plan, company data specifically for products in this category, as well as results of computer modeling using ECOSAR for selected chemical components of products in this category [ECOSAR is an aquatic toxicity modeling program and is a subroutine contained in EPIWIN model]. Although there are insufficient data to confirm that a similar pattern of alga toxicity exists, based on the fish and invertebrate data, a similar increasing level of toxicity is expected from the lower to higher molecular weight products. Proposed testing will develop the data needed to confirm this expectation. Based on the existing data, products in the Alkyl Alcohols C6 - C13 Category demonstrate a moderate to high degree of aquatic toxicity from the low to high molecular weight products, respectively.

Fish Acute Toxicity

TEST	Hexanol, branched and linear	Alcohols C6-8, branched	Alcohols C7-9, branched	Alcohols C8-10 iso, C9 rich	Alcohols C9-11 iso, C10 rich	Alcohols C11-14 iso, C12 rich,	Alcohols C11-14 iso, C13 rich
FISH ACUTE TOXICITY (96-hour)	LC_{50}= 97.7 mg/L (Brooke, 1984)	LC_{50}= 34.5 mg/L (Geiger, 1986)	LC_{50}= 14.0 mg/L (Geiger, 1988)	LC_{50}= 10.1 mg/L (EBSI, 1996a)	LC_{50}= 3.1 mg/L (EBSI, 1996b)	LC_{50}= 1.2 mg/L (EBSI, 1997c)	LC_{50}= 0.42 mg/L (EBSI, 1998a)

RA read across

Acute experimental toxicity test results are reported for rainbow trout (*Oncorhynchus mykiss*) and fathead minnow (*Pimephales promelas*). Hexanol, branched and linear, through C11-14 iso, C13 rich, alkyl alcohol products have the potential to cause acute toxicity (96-hour LC_{50}) within a range of approximately 98 to 0.4 mg/L.

Invertebrate Acute Toxicity

TEST	Hexanol, branched and linear	Alcohols C6-8, branched	Alcohols C7-9, branched	Alcohols C8-10 iso, C9 rich	Alcohols C9-11 iso, C10 rich	Alcohols C11-14 iso, C12 rich,	Alcohols C11-14 iso, C13 rich
DAPHNID ACUTE TOXICITY (48-hour)	RA	LC_{50}= 63 mg/L (Canton, 1978)	LL_{50}= 31.8 mg/L (Union Carbide, 1980)	LC_{50}= 4.9 mg/L (EBSI, 1996c)	RA	LC_{50}= 0.81 mg/L (EBSI, 1997d)	LC_{50}= 0.71 mg/L (EBSI, 1987)
DAPHNID ACUTE TOXICITY (48-hour)**	C6 OH LC_{50}= 137 mg/L (ECOSAR, 1999)	C7 OH LC_{50}= 56 mg/L (ECOSAR, 1999)	C8 OH LC_{50}= 22 mg/L (ECOSAR, 1999)				

** ECOSAR modeled data
OH alcohol

Experimental and modeled data show that these products have the potential to cause acute toxicity (48-hour EL_{50} or EC_{50}) within a range of approximately 137 to 0.7 mg/L. Acute experimental toxicity test results for five alkyl alcohol products are reported for a Daphnid (*Daphnia magna*). Experimental data for the hexanol, branched and linear, product are not available, but results from ECOSAR (1999), an aquatic toxicity computer model, can be used to adequately characterize the aquatic toxicity of this product.

Results of computer modeling for a C7 and C8 branched alcohol are consistent with the experimental data used to characterize the toxicity of the C6-8 and C7-9 branched alcohol products. This suggests that the ECOSAR model is sufficiently robust to accurately calculate the toxicity of this range of chemicals. Therefore, the modeled value for a C6 alcohol is expected to be consistent with an experimental value for a hexanol, branched and linear, product and will be used to characterize the range of Daphnid acute toxicity for the Alkyl Alcohol C6 - C13 Category. The Kow values used to

calculate the toxicity values for the C6, C7, and C8 alcohols were 1,75, 2,24, and 2,73, respectively. These values were calculated using the EPIWIN (1999) computer model.

Alga Toxicity

TEST	Hexanol, branched and linear	Alcohols C6-8, branched	Alcohols C7-9, branched	Alcohols C8-10 iso, C9 rich	Alcohols C9-11 iso, C10 rich	Alcohols C11-14 iso, C12 rich,	Alcohols C11-14 iso, C13 rich
ALGA TOXICITY (96-hour)	TESTING PROPOSED	RA	RA	LC_{50}= 8.5 mg/L (Bringmann, 1980)	RA	RA	TESTING PROPOSED

RA read across

An acute experimental toxicity threshold value is reported for the freshwater alga (*Scenendesmus quadricauda*) and used as read across data to the C8-10 iso, C9 rich alkyl alcohol product. This result suggests that the C9-11, C10 rich, alkyl alcohol has the potential to cause acute toxicity (based upon cell growth) at a concentration of above 8.5 mg/L. However, this study is not sufficient to adequately characterize the toxicity of products in this category to an alga.

ExxonMobil Chemical believes that the alga toxicity of the Alkyl Alcohols C6-C13 Category should be characterized by developing data for the hexanol, branched and linear, and the C11-14 iso, C13 rich, alkyl alcohol products to adequately characterize this endpoint. Data from fish and invertebrate acute toxicity studies show a consistent trend of increasing toxicity as carbon number and molecular weight increases. Acute toxicity to an alga is expected to follow the same trend and the proposed testing should appropriately define that range of toxicity. The one experimental value identified above will provide an intermediate toxicity value, which in conjunction with results from the proposed testing should provide adequate data to demonstrate an increasing range of alga toxicity for products in this category.

E. Environmental Fate

Biodegradation data are available for four alkyl alcohol products. They show that these alcohol products have the potential to biodegrade to a great extent within a standard 28-day test duration, which suggests that products in this category will not persist in the environment.

Although there is some information on photodegradation and fugacity, a complete data set to adequately characterize the alkyl alcohol products does not exist. Chemical equilibrium models are used to calculate fugacity, which describes the potential of a chemical to partition in the environment. These data can only be calculated. Preliminary information for selected component chemicals of products in the Alkyl Alcohol C6 - C13 Category suggests that these products are expected to partition primarily to water and soil. However, their fate in air is of environmental interest (this is discussed below under photodegradation). In addition, the majority of the component chemicals in these products have relatively low K_{ow} values, which suggests that they will

not tend to partition to suspended organic matter in air and precipitate to aquatic and terrestrial environmental compartments to a significant extent.

Biodegradation

TEST	Hexanol, branched and linear	Alcohols C6-8, branched	Alcohols C7-9, branched	Alcohols C8-10 iso, C9 rich	Alcohols C9-11 iso, C10 rich	Alcohols C11-14 iso, C12 rich,	Alcohols C11-14 iso, C13 rich
28-Day Aerobic Biodegradation Test	RA	RA	82% (EBSI, 1996d)	RA	71.1% (EBSI, 1997e)	59% (EBSI, 1997f)	58% (EBSI, 1998b)

RA read across

C7-C9 branched, and C9-C11 branched alkyl alcohol products have been shown to biodegrade rapidly using a 28-day standard biodegradation test procedure. In comparison, C11-C14 iso, C12 rich, and C11-C14 iso, C13 rich alkyl alcohol products biodegrade to slightly lower but significant extents, which suggests that although they are not expected to degrade at rates equivalent to the lighter alkyl alcohol products, they will not persist in the environment.

Upon review of the available information, sufficient quality data were identified to accurately characterize the biodegradability of the products in this category. The data show that these products can biodegrade to an extent ranging from approximately 58 to 82% after 28 days. These data were developed using non acclimated inocula obtained from wastewater treatment plants. The tests used closed systems, which is required when assessing the biodegradability of potentially volatile materials like those in this category. The test systems were continuously stirred, which is also recommended when evaluating mixtures containing several chemicals, some of which may have minimal water-solubility.

Photodegradation – Photolysis (Direct)

Direct photochemical degradation occurs through the absorbance of solar radiation by a chemical substance. If the absorbed energy is high enough, then the resultant excited state of the chemical may undergo a transformation. Simple chemical structures can be examined to determine whether a chemical has the potential for direct photolysis in water. First order reaction rates can be calculated for some chemicals that have a potential for direct photolysis using the procedures of Zepp and Cline (Zepp, 1977). UV light absorption of the chemical components in this category will be evaluated to identify those having the potential to degrade in solution. For those compounds with a potential for direct photolysis in water, first order reaction rates will be calculated. A technical document will be prepared that summarizes the results of information developed for this endpoint.

Photodegradation – Atmospheric Oxidation (Indirect)

Photodegradation can be measured (US EPA, 1999a) (EPA identifies OECD test guideline 113 as a test method) or estimated using models accepted by the EPA (US EPA, 1999b). An estimation method accepted by the EPA includes the calculation of atmospheric oxidation potential (AOP).

Atmospheric oxidation as a result of hydroxyl radical (OH-) attack is not direct photochemical degradation, but rather indirect degradation. AOPs can be calculated using a computer model. Alkyl alcohol products, such as those in this category, have the potential to volatilize to air. Preliminary data suggest that the potential ranges from moderate to low for the chemical components of products in this category. In air, those chemicals with a higher potential to volatilize may undergo reaction with photosensitized oxygen in the form of ozone and hydroxyl radicals.

The computer program AOPWIN (atmospheric oxidation program for Microsoft Windows) (EPIWIN, 1999) is used by OPPTS (Office of Pollution Prevention and Toxic Substances). This program calculates a chemical half-life based on an overall OH- reaction rate constant, a 12-hr day, and a given OH- concentration. This calculation will be performed for the representative chemical components in this category and summarized in robust summaries for this group of products.

Stability in Water (Hydrolysis)

Hydrolysis of an organic chemical is the transformation process in which a water molecule or hydroxide ion reacts to form a new carbon-oxygen bond. Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (Neely, 1985). Stability in water can be measured (US EPA, 1999a) (EPA identifies OECD test guideline 111 as a test method) or estimated using models accepted by the EPA (US EPA, 1999b).

All of the chemical structures included in this category are alkyl alcohols. As such they are not expected to hydrolyze at a measurable rate. A technical document will be prepared that discusses the nature of the chemical bonds present and the potential reactivity of this class of chemicals with water. This information will be summarized in robust summaries for this group of products.

Chemical Transport and Distribution In The Environment (Fugacity Modeling)

Fugacity based multimedia modeling can provide basic information on the relative distribution of chemicals between selected environmental compartments (i.e., air, soil, sediment, suspended sediment, water, biota). The US EPA has acknowledged that computer modeling techniques are an appropriate approach to estimating chemical partitioning (fugacity is a calculated endpoint and is not measured). A widely used fugacity model is the EQC (Equilibrium Criterion) model (Mackay, 1996). EPA cites the use of this model in its document titled *Determining the Adequacy of Existing Data* (US EPA, 1999a), which was prepared as guidance for the HPV Program.

In its document, EPA states that it accepts Level I fugacity data as an estimate of chemical distribution values. The input data required to run a Level I model include basic physicochemical parameters; distribution is calculated as percent of chemical partitioned to 6 compartments (air, soil, water, suspended sediment, sediment, biota) within a unit world. Level I data are basic partitioning data that allow for comparisons between chemicals and indicate the compartment(s) to which a chemical is likely to partition.

The EQC Level I is a steady state, equilibrium model that utilizes the input of basic chemical properties including molecular weight, vapor pressure, and water solubility to calculate distribution within a standardized regional environment. This model will be used to calculate distribution values for representative chemical components identified in products in this category. A computer model, EPIWIN – version 3.02 (EPIWIN, 1999), will be used to calculate the properties needed to run the Level I EQC model. This information will be summarized in robust summaries for this group of products.

IV. TEST PLAN SUMMARY

ExxonMobil Chemical believes that the Alkyl Alcohols C6 - C13 Category of products should be further examined in the following manner:

- Calculate physicochemical data as described in the EPA document titled, *The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program* for selected chemical components of the alkyl alcohol products in this category. Provide measured data for selected products where readily available.
- Prepare a technical discussion on the potential of alkyl alcohol products in this category to photodegrade. Calculate AOP values for selected chemical components of alkyl alcohol products in this category.
- Prepare a technical discussion on the potential of alkyl alcohol products in this category to hydrolyze.
- Calculate fugacity data for selected chemical components of alkyl alcohol products in this category.
- Conduct two acute algal toxicity assays, one with a hexanol, branched and linear, and a second with an alcohol C11-C14, C13 rich, products.
- Conduct one mouse micronucleus assay with a alkyl alcohol C6 product.

ExxonMobil Chemical Company believes the thorough evaluation of the strategic anchor studies, the development of selected information and data, and the overall robustness of the final screening data set for an Alkyl Alcohols C6 -C13 Category complies with the objectives of the HPV Chemical Challenge program.

REFERENCES

Brooke, L.T., D.J. Call, Geiger, D.L. and C.E. Northcott, (1984). "Acute Toxicities of Organic Chemicals to Fathead Minnows (*Pimephales promelas*). Vol. 1. Center for Lake Superior Environmental Studies. University of Wisconsin-Superior, Superior, WI. Pp. 179-180.

Bringmann, G. and R. Kühn. (1980). "Comparison of the Toxicity Thresholds of Water Pollutants to Bacteria, Algae, and Protozoa in the Cell Multiplication Inhibition Test." Water Research **14**: 231-241.

Canton, J.H., and D.M.M. Adema. (1978). "Reproducibility of Short-term and Reproduction Toxicity Experiments with *Daphnia magna* and Comparison of the Sensitivity of *Daphnia magna* with *Daphnia pulex* and *Daphnia cucullata* in Short-term Experiments." Hydrobiologica **59(2)**: 135-140.

EPIWIN, (1999). Estimation Program Interface for Windows, version 3.02. Syracuse Research Corporation, Syracuse, NY, USA.

Esso Research and Engineering (1960a). Acute Oral Toxicity of Isodecanol in Rats. Unpublished report.

Esso Research and Engineering (1960b). Acute Dermal Toxicity of Isodecanol in Rabbits. Unpublished report.

Esso Research and Engineering Company (1961a). Repeat Dermal Application of Hexyl Alcohol. Unpublished report.

Esso Research and Engineering Company (1961b). Repeat Dermal Application of Isooctyl Alcohol. Unpublished report.

Esso Research and Engineering (1968a), Histopathological Evaluation. Supplement to Repeated Dermal Application Report. Unpublished report.

Esso Research and Engineering (1968b). Acute Oral Toxicity of Isononyl Alcohol in Rats. Unpublished report.

Esso Research and Engineering (1968c). Acute Dermal Toxicity of Isononyl Alcohol in Rabbits. Unpublished report.

Esso Research and Engineering (1979a). Acute Oral Toxicity Study of Isoheptyl Alcohol in Rats. Unpublished report.

Esso Research and Engineering (1979b). Acute Dermal Toxicity of Isoheptyl Alcohol in Rabbits. Unpublished report.

Esso Research and Engineering (1980). Acute Inhalation Toxicity of Isoheptyl Alcohol in Rats, Mice, and Guinea Pigs. Unpublished report.

European Chemicals Bureau (ECB) (2000a). IUCLID Data Set, Hexan-1-ol (CAS#: 111-27-3).

European Chemicals Bureau (ECB) (2000b). IUCLID Data Set, 2-ethylhexan-1-ol (CAS#: 104-76-7).

European Chemicals Bureau (ECB) (2000c). IUCLID Data Set, Dodecan-1-ol (CAS#: 112-53-8).

Exxon Biomedical Sciences, Inc. (EBSI) (1987). A Static Acute *Daphnia* Toxicity Test. Unpublished report.

Exxon Biomedical Sciences, Inc. (EBSI) (1994a). Developmental Toxicity Study of Isooctyl Alcohol in Rats. Unpublished report.

Exxon Biomedical Sciences, Inc. (EBSI). 1994b. East Millstone, NJ, USA. Microbial Mutagenesis in Salmonella Mammalian Microsome Plate Incorporation Assay with C7-C9 Branched Alkyl Acetate Ester. Unpublished report.

Exxon Biomedical Sciences, Inc. (EBSI), 1994c. East Millstone, NJ, USA. Microbial Mutagenesis in Salmonella Mammalian Microsome Plate Incorporation Assay with C11-C14 Branched Alkyl Acetate Ester. Unpublished report.

Exxon Biomedical Sciences, Inc. (EBSI). 1994d. East Millstone, NJ, USA. In Vivo Mammalian Bone Marrow Micronucleus Assay Oral Gavage Dosing Method with C7-C9 Branched Alkyl Acetate Ester. Unpublished report.

Exxon Biomedical Sciences, Inc. (EBSI), 1994e. East Millstone, NJ, USA. In Vivo Mammalian Bone Marrow Micronucleus Assay Oral Gavage Dosing Method with C11-C14 Branched Alkyl Acetate Ester. Unpublished report.

Exxon Biomedical Sciences, Inc. (EBSI), 1995a. East Millstone, NJ, USA. Microbial Mutagenesis in Salmonella Mammalian Microsome Plate Incorporation Assay with C6 Branched and Linear Alkyl Acetate Ester. Unpublished report.

Exxon Biomedical Sciences, Inc. (EBSI), 1995b. East Millstone, NJ, USA. In Vitro Chromosomal Aberration Assay in CHO Cells with C6 Branched and Linear Alkyl Acetate Ester. Unpublished report.

Exxon Biomedical Sciences, Inc. (EBSI) (1996a). Fish Acute Toxicity Test. Unpublished report.

Exxon Biomedical Sciences, Inc. (EBSI) (1996b). Fish Acute Toxicity Test. Unpublished report.

Exxon Biomedical Sciences, Inc. (EBSI) (1996c). Acute Toxicity for *Daphnia*. Unpublished report.

Exxon Biomedical Sciences, Inc. (EBSI) (1996d). Ready Biodegradability: OECD 301F Manometric Respirometry Test. Unpublished report.

Exxon Biomedical Sciences, Inc. (EBSI) (1997c). Fish Acute Toxicity Test. Unpublished report.

Exxon Biomedical Sciences, Inc. (EBSI) (1997d). Acute Toxicity for *Daphnia*. Unpublished report.

Exxon Biomedical Sciences, Inc. (EBSI) (1997e). Ready Biodegradability: OECD 301F Manometric Respirometry Test. Unpublished report.

Exxon Biomedical Sciences, Inc. (EBSI) (1997f). Ready Biodegradability: OECD 301F Manometric Respirometry Test. Unpublished report.

Exxon Biomedical Sciences, Inc. (EBSI) (1998a). Fish Acute Toxicity Test. Unpublished report.

Exxon Biomedical Sciences, Inc. (EBSI) (1998b). Ready Biodegradability: OECD 301F Manometric Respirometry Test. Unpublished report.

Exxon Biomedical Sciences, Inc. (EBSI) (1998c). N-Octanol/Water Partition Coefficient. Unpublished report.

Geiger, D.L., D.J. Call, and L.T. Brooke. (1988). "Acute Toxicities of Organic Chemicals to Fathead Minnows (*Pimephales promelas*). Vol. 4. Center for Lake Superior Environmental Studies. University of Wisconsin-Superior, Superior, WI. Pp. 183-184.

Geiger, D.L., S.H. Poirier, L.T. Brooke, and D.J. Call. (1986). "Acute Toxicities of Organic Chemicals to Fathead Minnows (*Pimephales promelas*). Vol. 3. Center for Lake Superior Environmental Studies. University of Wisconsin-Superior, Superior, WI. Pp. 181-182.

Hazleton Labs (1960) "Acute oral, acute dermal, and acute inhalation toxicity of Hexyl alcohol, Isoheptyl alcohol, and Isooctyl Alcohol." Unpublished report.

Hazleton Laboratories Incorporated (HLI), (1963) Falls Church, VA, USA. Unpublished report.

Klimisch, H. J., M. Andreae, and U. Tillmann, (1997). A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data. Regulatory Toxicology and Pharmacology. 25:1-5.

Lington, A.W. and Bevan, C., (1994). Patty's Industrial Hygiene and Toxicology, Fourth Edition, John Wiley & Sons, Inc, Chapter Thirty, "Alcohols," pp. 2585-2710.

Mackay, D., A. Di Guardo, S. Paterson, and C. E. Cowan, (1996). Evaluating the Environmental Fate of a Variety of Types of Chemicals Using the EQC Model. Environ. Toxicol. Chem. 15:1627-1637.

Mann, A.H., (1987). An assessment of the likely metabolic fate of some isomers of hexyl acetate. The Robins Institute of Industrial & Environmental Safety, University of Surrey, Guildford Surrey, U.K.

Monick, J.A., (1968). Alcohols. Their Chemistry, Properties and Manufacture. Reinhold Book Corporation, NY.

Neely, W. B., (1985). Hydrolysis. In: W. B. Neely and G. E. Blau, eds. Environmental Exposure from Chemicals. Vol I., pp. 157-173. CRC Press, Boca Raton, FL, USA.

Nelson, B.K., Brightwell, W.W., Khan, A., Krieg, E.F., Jr., Hoberman, A.M., (1989). "Developmental toxicology evaluation of 1-pentanol, 1-hexanol, and 2-ethyl-1-hexanol administered by inhalation to rats." Journal of the American College of Toxicology **8(2)**: 405-410. NIOSH, Division of biomedical and behavioral sciences.

Nelson, B.K., Brightwell, W.W., Khan, A., Krieg, E.F., Jr., Hoberman, A.M., (1990). "Developmental toxicology assessment of 1-Octanol, 1-Nonanol, and 1-Decanol administered by inhalation to rats." Journal of the American College of Toxicology **9(1)**: 93-97.

RCC Research and Consulting Co. (1988a) "Acute oral toxicity study with Isooctyl Alcohol in rats." Unpublished report.

RCC Research and Consulting Co., (1988b) "Acute Oral Toxicity Study Isododecanol in Rats." Unpublished report.

RCC Research and Consulting Co., (1988c) "Acute Oral Toxicity of Tridecyl Alcohol Study in Rats." Unpublished report.

Rhodes, C., Soames, T., Stonard, M.D., Simpson, M.G., Vernall, A.J., Elcombe, C.R, (1984). "The absence of testicular atrophy and in vivo and in vitro effects on hepatocyte morphology and peroxisomal enzyme activities in male rats following the administration of several alkanols," Toxicology Letters 21: 103-109.

Shimizu, H., Suzuki, Y., Takemura, N., Goto, S., Matsushita, H., (1985) "The Results of Microbial Mutation Test for Forty-Three Industrial Chemicals," *Japanese Journal of Industrial Health*, 27: 400-419.

US EPA TSCA 8(e) Submission: (1989a) Study of the Prenatal Toxicity of Isononylalcohol 1 and Isononylalcohol 2 in Rats After Oral Administration (Gavage); EPA OTS Doc #: 89-910000247.

US EPA TSCA 8(e) Submission: (1989b) Study of the Prenatal Toxicity of Isodecanol, 2-Ethylhexanol, and 711 Alcohol (T.C.) in Rats After Oral Administration (Gavage); EPA OTS Doc #: 89-910000245.

Union Carbide Corp. (1980). "The Acute Toxicity of MRD-80-4 to the Water Flea (*Daphnia magna* Straus)." Unpublished report.

US EPA, (1999a). Determining the Adequacy of Existing Data. OPPT, EPA., Washington, DC, USA.

US EPA, (1999b). The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program. OPPT, EPA, Washington, DC, USA.

Wislocki, P.G., Miwa, G.T., and Lu, A.Y.H., (1980). Reactions Catalyzed by the Cytochrome P-450 System. Enzymatic Basis of Detoxification. Vol. I (ed. W.B.Jakoby), Academic Press, New York, NY.

Zepp, R. G., and D. M. Cline, (1977). Rates of Direct Photolysis in the Aqueous Environment. Environ. Sci. Technol. 11:359.366.

Table 3. Assessment Plan for the Alkyl Alcohols C6-C13 Category Under the Program. (Robust summaries for existing studies are submitted separately.)

Stream Description	Human Health Effects						Ecotoxicity			Environmental Fate				
	Acute Toxicity	Genetic Point Mut.	Genetic Chrom.	Sub-chronic	Develop-mental	Reproduction	Acute Fish	Acute Invert.	Algal Toxicity	Physical Chem.[1]	Photo-deg.	Hydro-lysis	Fugacity	Biodeg.
Hexyl alcohol	A	A	T	A	A	A	A	CM	T	CM	TD	TD	CM	RA
Alkyl alcohol C6-8, branched	A	RA	RA	RA	RA	RA	A	A	RA	CM	TD	TD	CM	RA
Alkyl alcohol C7-9, branched	A	A	A	A	A	A	A	A	RA	CM	TD	TD	CM	A
Alkyl alcohol C8-10, branched	A	RA	RA	A	A	A	A	A	A	CM	TD	TD	CM	RA
Alkyl alcohol C9-11, branched	A	RA	RA	RA	A	A	A	RA	RA	CM	TD	TD	CM	A
Alkyl alcohol C11-14, branched	A	A	A	A	RA	RA	A	A	T	CM	TD	TD	CM	A

1 Measured data for selected physicochemical endpoints will be identified in conjunction with calculated data to characterize this category.

A Adequate existing data available TD Technical Discussion proposed RA Read Across (see Sec. III.B)

CM Computer Modeling proposed T Testing proposed

NA Not Applicable